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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/921,819	08/03/2001	Roland Buelow	39691-0005A	8351

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EXAMINER

WEHBE, ANNE MARIE SABRINA

ART UNIT	PAPER NUMBER
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1633

DATE MAILED: 07/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

**Advisory Action
Before the Filing of an Appeal Brief**

Application No.

09/921,819

Applicant(s)

BUELOW ET AL.

Examiner

Anne Marie S. Wehbe

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--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 23 June 2005 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The reply was filed after the date of filing a Notice of Appeal, but prior to the date of filing an appeal brief. The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☒ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
(a) ☒ They raise new issues that would require further consideration and/or search (see NOTE below);
(b) ☐ They raise the issue of new matter (see NOTE below);
(c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
(d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: See Continuation Sheet. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☒ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: _____.

Claim(s) objected to: _____.

Claim(s) rejected: 13-30, 67-72, 76.

Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing of good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: see attached sheets.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). _____.
13. ☐ Other: _____.

Attachment to Advisory Action

3(a) cont. Claim 27 has been amended to include new limitations not previously present in these claims. The new limitations include that the DNA fragment to be used in the method contains regulatory sequences from a non-human animal and that the human Ig gene segment is flanked by non-coding sequences from the non-human animal. These limitations are new in the context of the method claims of 27-30 and would require further search and consideration.

11. cont. Applicant's arguments have been fully considered but have not been found persuasive in overcoming the rejections of record as discussed below.

As a first issue, the applicants request the withdrawal of finality of the previous office action because in their opinion the new grounds of rejection could have been made in the first office action and were not necessitated by applicant's amendment. In response, the office finds that the finality of the previous office action was and is proper. The final office action was prepared based on the amended claim set received by the office on 12/16/04. In this amendment, the applicant added new claims 67-72 and 76 not previously considered which contained claim limitations not present in the original set of claims examined in the first office action. Thus, rejections of new claims 67-72 and 76 were clearly necessitated by applicant's amendments. Further, the 12/16/04 amendment amended independent claims 13 and 27 to further limit the claimed transgenic vectors to comprising non-human Ig sequences derived from a non-human animal "other than a bird". The claims as originally filed and examined in the first office action read broadly on non-human sequences from any animal capable of undergoing gene conversion.

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Note as well that claim 15 as originally filed clearly claimed that the non-human animal was a chicken. Applicant's amendment of 12/16/04 further amended claim 15 to delete the limitation to chicken. Thus, the claims as originally examined encompassed sequences from birds and more particularly appeared to be directed to sequences from birds such as chickens. The amended claim set excluded this subject matter. Therefore, new rejections were required, based on applicant's amendments. Furthermore, regarding applicant's contention that the rejections based on Lonberg or Rader "could" have been made previously, MPEP 903.04 states, "The examiner is not called upon to cite *all* references that may be available, but only the "best." (37 CFR 1.104(c).) Multiplying references, any one of which is as good as, but no better than, the others, adds to the burden and cost of prosecution and should therefore be avoided." In considering the applicant's disclosure, it is noted that the specification, which broadly disclosing Ig sequences from non-human gene conversion animals, includes specific examples of transgenic chickens. Amending the claims to exclude birds thus necessitated new grounds of rejection. Therefore, the office upholds the finality of the previous office action.

In regards to the rejection of claim 76 under 35 U.S.C. 102(a) as anticipated by Rader et al., this rejection is maintained because the after-final amendment has not been entered which proposed the cancellation of this claim.

In regards to the rejection of claims 13-26 and 67-71 under 35 U.S.C. 102(b) as anticipated by Lonberg et al., the rejection of record stands. Applicant's arguments concerning the proposed amendments to the claims is not persuasive as the claim amendments have not been entered. However, applicant's arguments as they apply to the claims finally rejected are addressed as follows. Applicant's argument that Lonberg did not recognize the significance of

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gene conversion in rabbits as opposed to gene rearrangement in mice and that Lonberg did not observe any gene conversion in humans or mice is not persuasive. While Lonberg exemplified transgenic vectors useful for making mice and transgenic mice comprising human Ig sequences, Lonberg further teaches transgenic vectors useful for making transgenic rabbits (Lonberg et al., column 10, lines 46-60). Rabbits produce immunoglobulin diversity using gene conversion. Since Lonberg specifically teaches producing vectors for expressing human Ig gene sequences in rabbits, Lonberg meets the claim limitations. There is no requirement that Lonberg recognize or teach the applicant's particular motivation for using rabbits versus mice. In addition, contrary to applicant's argument, Lonberg et al. does in fact teach the human Ig gene segments are flanked and separated by non-coding sequences derived from the non-human animal. As stated in the rejection of record, Lonberg teaches that non-coding switch regions flanking the human constant region gene or genes are derived from those that occur naturally in the germline of the species that is to receive the transgene construct, i.e. a rabbit, and further that additional regulatory sequences in the transgene are also derived from the non-human animal (Lonberg et al., column 8, lines 19-21, and column 9, lines 3-6). Therefore, applicant's argument are not found persuasive and the rejection of record is maintained.

In regards to the rejection of claims 27-30 under 35 U.S.C. 103(a) over Fell et al. in view of Rader et al., the rejection is maintained because the proposed amendments have not been entered and applicant's arguments are based on the proposed amended claims.

In regards to the rejection of claims 67-72 under 35 U.S.C. 112, second paragraph. The after-final arguments do not address this rejection. Further, the proposed amendment has not been entered.

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Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. The examiner can be reached Monday- Friday from 10:30-7:00 EST. If the examiner is not available, the examiner's supervisor, Dave Nguyen, can be reached at (571) 272-0731. For all official communications, **the new technology center fax number is (571) 273-8300**. Please note that all official communications and responses sent by fax must be directed to the technology center fax number. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737.

Dr. A.M.S. Wehbé

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER

A handwritten signature in black ink, appearing to be 'Anne M. Wehbé', with a long horizontal line extending from the end of the signature.